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1: Protein Sci. 1999 Dec;8(12):2589-97.

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The structures of the neurotrophin 4 homodimer and the brain-derived neurotrophic factor/neurotrophin 4 heterodimer reveal a common Trk-binding site.

Robinson RC, Radziejewski C, Spraggon G, Greenwald J, Kostura MR, Burtnick LD, Stuart DI, Choe S, Jones EY.

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The neurotrophins are growth factors that are involved in the development and survival of neurons. Neurotrophin release by a target tissue results in neuron growth along the neurotrophin concentration gradient, culminating in the eventual innervation of the target tissue. These activities are mediated through trk cell surface receptors. We have determined the structures of the heterodimer formed between brain-derived neurotrophic factor (BDNF) and neurotrophin 4 (NT4), as well as the structure of homodimer of NT4. We also present the structure of the Neurotrophin 3 homodimer, which is refined to higher resolution than previously published. These structures provide the first views of the architecture of the NT4 protomer. Comparison of the surface of a model of the BDNF homodimer with the structure of the neurotrophin homodimers reveals common features that may be important in the binding between the neurotrophins and their receptors. In particular, there exists an analogous region on the surface of each neurotrophin that is likely to be involved in trk receptor binding. Variations in sequence on the periphery of this common region serve to confer trk receptor specificity.

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